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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
WEGERT, SANDRA L	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 05/18/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/944,954	BEART ET AL.	
	Examiner	Art Unit	
	Sandra Wegert	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-27* is/are pending in the application.

4a) Of the above claim(s) *25-27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *01 September 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *5/2703*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Detailed Action

Status of Application, Amendments, and/or Claims

The Information Disclosure Statement, sent 27 May 2003, has been entered into the record. Applicant's election of Invention I with a Species of the chemical genus found in Figure 6A, as well as a Species of glutamate transporter (EAAT1), in the Paper of 10 November 2003, is acknowledged. Applicant argued that all three Inventions could be examined together without undue burden to the Examiner. However, Inventions I, II and III were properly restricted as separate inventions having separate uses and producing different results or products. The methods and products of Inventions I-III are independent and distinct, each from the other, because the methods are practiced with materially different process steps for materially different purposes and each method requires a non-coextensive search because of different starting materials, process steps and goals. Invention I is a competitive binding assay, used to find substrates of a glutamate transporter. Invention II encompasses the products produced by the binding assay of Invention I and is related to Invention I as a product is related to the process that produces it. Invention III is a method of treating animals for a glutamate transporter-related disorder. Each invention requires different starting materials, different methods, different personnel, and different chances of success. Claims 25-27 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected Invention, there being no allowable generic or linking claim.

Claims 1-24 are under examination in the Instant Application.

Informalities

Specification

The disclosure is objected to because of the following informalities:

Abstract

The abstract of the disclosure is objected to because it consists of 219 words (see MPEP § 608.01(b)). The Abstract should consist of a single paragraph of 150 words or less.

Appropriate correction is required.

Claim Rejections/Objections

Claim Objections

Claim 13 is objected to because it does not end in a period. All Claims must end in a period (see MPEP § 609.01(m)).

Appropriate correction is required.

Claim Rejections- 35 USC § 112, first paragraph – Enablement.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> **The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.**

Claims 1-24 are rejected under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement for a method of identifying compounds that bind to or modulate glutamate transporters. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 1-24 are drawn to a competitive binding assay used for the purpose of identifying compounds that bind to or modulate glutamate transporters. Dependent claims specify the receptor compounds tested as well as the simultaneous use of the low-affinity Glutamate receptor compound 4-MG (4-methyl glutamate) in some experiments. Other dependent claims specify use of GLAST, GLT1, EAAT1 or EAAT2 transporters, which are well-characterized in the literature (Slotboom, et al, 1999, Microbiol. Mol. Biol. Rev., 63(2): 293-307). The Specification discloses the results of assays that measured the binding of several receptor compounds to homogenates of rat brain cortex. Figure 5 of the instant Specification shows that receptor compounds bind with high affinity to rat brain homogenates and that this binding is differentially affected by the presence of 4-MG. However, Applicants have failed to demonstrate that the competitive binding assay described is limited to or encompasses glutamate *transporters.*

Applicants used membrane fractions of rat cortex to perform standard in vitro binding assays. They also used 4-MG to purportedly limit the influence of the low affinity transporters. 2S, 4R-4-Methyglutamate (4-methyl glutamate or 4-MG) is a desensitizer at the low affinity kainate receptor, so it is often used as a tool for distinguishing between and among the different glutamate *receptors* in brain homogenates (Carroll, et al, 1988, Neurosci. Lett., 255: 71-74; Toms, et al, 1997,

Neuropharmacol., 36: 1483-1488). However, applicants have claimed its use in assays that measure binding of compounds to glutamate *transporters,* without confirming the presence of the transporters of interest in the brain homogenates or using parallel techniques that would differentiate glutamate transporters from receptors, and thus distinguish the results obtained in the instant disclosure from the substantial literature in which similar or identical assays are performed on glutamate receptors (see, for example, Vandenberg, et al, 1997, Mol. Pharmacol., 51: 809-815 and, Toms, et al, 1997, Neuropharmacol., 36: 1483-1488). The results obtained might very well be due primarily or entirely to brain glutamate receptor*s*. In fact, Applicants utilized glutamate receptor compounds for the assays, rather than glutamate transporter substrates, giving further weight to the argument that the instant Specification describes glutamate receptor binding assays.

In summary, the specification does not provide a description of a repeatable process of detecting compounds that bind to or modulate glutamate transporters. In addition, the predictability of the art is low with regard to methods that distinguish between glutamate receptor binding and glutamate transporter binding in assays using whole brain homogenates. For this reason undue experimentation would be required to identify glutamate transporter binding compounds using the techniques described.

Due to the large quantity of experimentation required to --determine how to identify an compounds that bind glutamate transporters in whole tissue, the lack of direction or guidance in the specification regarding same (e.g., the lack of guidance regarding the functional isolation of glutamate transporters in whole-brain isolates), the lack of working examples in which specific glutamate transporter antagonists or

substrates are used or the transporters are isolated before being used in the binding assays, and the state of the art showing the unpredictability of the numbers and types of glutamate receptors and transporters in a tissue-- undue experimentation would be required of the skilled artisan to use the claimed invention in its full scope.

35 USC § 112, first paragraph – Written Description.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> **The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.**

Claims 1-24 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

Claims 1-24 are directed to methods of identifying compounds that bind to or modulate glutamate transporters. Further, the claims recite use of GLAST, GLT1, EAAT1 or EAAT2 transporters, as well as the low-affinity receptor antagonist 4-MG. Figures 6A-6I list the species of small alkyl and alkenyl derivatives that might be used as competitive binding compounds.

The specification teaches the results of binding assays performed on rat cortical homogenates using glutamate receptor compounds as binding modifiers or competitive antagonists (see, Figure 5). However, the specification does not teach a method that

identifies glutamate transporter modulators. The description of a whole tissue binding assay in a tissue in which are found both glutamate transporters and glutamate receptors, is not adequate written description of a method of identifying ligands for transporters.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed"* (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (See *Vas-Cath* at page 1116).

With the exception of the method referred to above, the skilled artisan cannot envision the methods that would enable the claimed invention, and therefore, would not know how to use them. Conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of use. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of use. The actual results are required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only a method that produces glutamate receptor modulators, but not the full breadth of the claims, meets the written description provision of 35 U.S.C. §112,

first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

35 USC § 112, second paragraph – Indefinite Terminology

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> **The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.**

Claims 13 and 15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 13 is rendered indefinite because the cited compound's molecular formula contains an undefined term ("p" at the end of Claim 13, in the phrase: "R^2 and R^3 taken together can be -CH2(CH2)pCH2-"). The metes and bounds of the claimed molecules, therefore, cannot be ascertained. This rejection can be overcome by supplying a definition of "p" within the claim.

Claim 15 is rendered indefinite because it claims "the receptor compound," but defines the receptor compound using four structural formulas. It it not known therefore, the metes and bounds of the compound as claimed. If the Applicant is claiming a mixture of compounds, the mixture must be defined as to the concentrations or relative weights of the components. Furthermore, Claim 15 indefinite because the cited compound's molecular formula contains an undefined term ("Ar" in the last structural formula). The metes and bounds of the claimed molecules, therefore, cannot be ascertained. This rejection can be overcome by supplying a definition of "Ar" within the claim.

Conclusion: Claims 1-24 are rejected for the reasons recited above.

Advisory information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sandra Wegert whose telephone number is (571) 272-0895. The examiner can normally be reached Monday - Friday from 9:00 AM to 5:00 PM (Eastern Time). If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Kunz, can be reached at (571) 272-0887.

The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SLW
4/29/04

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